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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/652,928	CHIAUR ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11,13,14 and 16-36* is/are pending in the application.

4a) Of the above claim(s) *1-6,11 and 17-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,13,14,16 and 29-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 February 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-7, 11, 13-14, and 16-36 pending in the application.

[2] Applicant's preliminary amendment to the claims, filed on 6/12/2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

Restriction/Election

[3] Applicant's election with traverse of Group X, original claims 7, 9, 13-14, and 16, in the reply filed on 6/12/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Original claim 9 has been canceled and new claims 29-36 depend from claims of the elected invention. Thus, claims 7, 13-14, 16, and 29-36 are being examined on the merits.

[4] Claims 1-6, 11, and 17-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/12/2006.

Priority

[5] Applicant's claim to domestic priority under 35 USC § 120 to US non-provisional application 09/385,219, filed on 8/27/1999, now US Patent 6,720,181, is acknowledged.

Applicant's claim to domestic priority under 35 USC § 119(e) to US provisional applications 60/098,355, filed on 8/28/1998, 60/118,568, filed on 2/3/1999, and 60/124,449, filed on 3/15/1999, is acknowledged.

[6] As noted in the prior Office action, in response to this Office action, applicant should amend the priority claim to include the status of the parent application, application 09/385,219, which, as noted above, is now US Patent 6,720,181.

Information Disclosure Statement

[7] It appears that no IDS has been filed in the instant application. If the examiner has inadvertently overlooked a previously filed IDS, applicant's cooperation is appreciated in alerting the examiner to this oversight.

Specification/Informalities

[8] The attempt to incorporate subject matter into this application by reference to a hyperlink embedded in the specification (for example, page 35, lines 19 and 33 and p. 89, lines 14-20) is improper. Incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01 regarding hyperlinks in the specification and 608.01(p), paragraph I regarding incorporation by reference. In view of the lengthy specification, applicant's cooperation is requested in identifying and appropriately correcting any other hyperlinks that may be present in the instant application. In view of the lengthy specification, applicant's cooperation is appreciated in

reviewing the specification for additional hyperlinks that may have been inadvertently overlooked by the examiner.

[9] This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicants should identify nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids in the specification by a proper sequence identifier, i.e., "SEQ ID NO:" (see MPEP 2422.01). If these sequences have not been listed in the computer readable form and paper copy of the sequence listing, applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See particularly p. 17, lines 10 and 16, p. 112, line 19, p. 117, lines 27-29, p. 127, lines 7, 10, and 32, and Figure 56A of the specification. In view of the lengthy specification, applicant's cooperation is appreciated in reviewing the specification for additional sequences that may have been inadvertently overlooked by the examiner.

Claim Objections

[10] Claim 7 is objected to in the recitation of "both Fbp1, βTrcp2, and IKBα" as the term "both" is used to refer to two objects, not three. Appropriate correction is required.

[11] Claim 34 is objected to as ending with two periods. It is suggested that applicant delete a period.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[12] Claims 7, 13-14, 16, and 29-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 7, 13 (claims 29, 31, 33, and 35 dependent therefrom), 14, and 16 (claims 30, 32, 34, and 36 dependent therefrom) are indefinite in the recitation of "Fbp1." While the specification provides a description of a protein referred to as "Fbp1" (specification at pp. 4-5), the prior art recognizes at least two other proteins that are also referred to as "Fbp1" that appear to be distinct in structure and function from the "Fbp1" protein described herein. See, *e.g.,* Angenent et al. (*Plant Cell* 4:983-993, 1992), which discloses a floral binding protein 1 and Antoniewski et al. (*Mol Cell Biol* 14:4465-4474, 1994), which discloses a fat body protein, both of which are referred to as "Fbp1." It is suggested that applicant clarify the meaning of the term "Fbp1."

[b] Claim 7, 13 (claims 29, 31, 33, and 35 dependent therefrom), 14, and 16 (claims 30, 32, 34, and 36 dependent therefrom) recite the limitation "the activity." There is insufficient antecedent basis for this limitation in the claims. Furthermore, it is unclear from the claims and the specification as to *the* activity that is intended as being encompassed by the claims. It is suggested that applicant clarify the meaning of the term "the activity."

[c] Claim 7, 13 (claims 29, 31, 33, and 35 dependent therefrom), 14, and 16 (claims 30, 32, 34, and 36 dependent therefrom) are indefinite in the recitation of "Fbp1" and "βTrcp2" as it is unclear from the specification and the claims as to the scope of polypeptides that are intended as being encompassed by the terms "Fbp1" and "βTrcp2." According to the specification, "Fbp1" and "βTrcp2" are polypeptides that belong to the F-box family of proteins (pp. 1-2 and 5). While the specification teaches properties of "Fbp1" and "βTrcp2" proteins (specification at pp. 4-5), it fails to define which of these characteristics are necessary for inclusion of a "Fbp1" or "βTrcp2" protein which is distinct from other Fbp or βTrcp proteins that are within the F-box protein family of proteins. It is suggested that applicant clarify the meanings of the terms "Fbp1" and "βTrcp2."

[d] Claim 14 (claims 16, 30, 32, 34, and 36 dependent therefrom) is confusing in that it is unclear in step c. as to which "test compound or compounds" are being tested for altering Fbp1 or βTrcp2 activity. For example, step a. recites "contacting a compound with a cell or cell extract expressing...a test compound, and detecting a change in the activity of Fbp1." Is the compound that is contacted with the cell, the test compound

expressed by the cell, or both compounds intended as being "the test compound or compounds" as recited in step c. of claim 14? It is suggested that applicant clarify the meaning of the claim. In the interest of advancing prosecution, the examiner has interpreted the term "the test compound or compounds" in step c. as being either of the compound that is contacted with the cell or the test compound expressed by the cell.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[13] Claims 7, 13-14, 16, and 29-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to screening assays that measure the change in "the activity" of a genus of "Fbp1" or "βTrcp2" proteins.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings,

or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of Fbp1 polypeptides, *i.e.,* SEQ ID NO:2 and only a single representative species of βTrcp2 polypeptides, *i.e.*, the βTrcp2 polypeptide disclosed by Kipreos and Pagano, *Genome Biol* 1:3002.1 (cited by applicant at p. 5, lines 16-17 of the specification). The specification fails to describe any additional representative species of the recited genus of polypeptides or activities thereof that can be detected. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the recited genus of polypeptides encompasses species that are widely variant. For example, the specification discloses that Fbp1 and βTrcp2 are F-box proteins (p. 5, line 25) and that the F-box proteins of the invention may be mutants, homologues, or allelic variants (specification at pp. 32-33 and 37), which could have any function or activity, including non-functional proteins. The

recitation of "Fbp1" or "βTrcp2" fails to provide a sufficient description of the recited genus of proteins as it merely describes the "functional" features of the genus without providing any definition of the structural features of the species within the genus. This functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus. *Regents of the University of California v. Eli Lilly*, (43 USPQ2d 1398). As such, the disclosure of the single representative species as noted above is insufficient to be representative of the attributes and features of all species encompassed by the recited genus of polypeptides.

Given the lack of description of a representative number of polypeptides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[14] Claims 7, 13-14, 16, and 29-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for detecting a change in the activity of Fbp1 of SEQ ID NO:2 and βTrcp2 as disclosed by Kipreos and Pagano (*supra*), does not reasonably provide enablement for a method of using all "Fbp1" and "βTrcp2" proteins as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: As noted above, the specification discloses that Fbp1 and βTrcp2 are F-box proteins (p. 5, line 25) and that the F-box proteins of the invention may be mutants, homologues, or allelic variants (specification at pp. 32-33 and 37). Thus, the claims have been interpreted as encompassing a method for detecting the activity of any Fbp1 and βTrcp2 proteins, including any mutants, homologues, or allelic

variants thereof having any activity. The enablement provided by the specification is not commensurate in scope with the claim with regard to the number of proteins and detectable activities thereof as encompassed by the claims. In this case, the specification is enabling only for methods for detecting a change in the activity of Fbp1 of SEQ ID NO:2 and βTrcp2 as disclosed by Kipreos and Pagano (*supra*).

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: The amino acid sequence of a polypeptide determines the its structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.*, multiple substitutions. At the time of the invention, methods for isolating or generating variants and mutants of a given polypeptide were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the polypeptide of SEQ ID NO:12 with an expectation of obtaining a polypeptide having the desired activity/utility. At the time of the invention,

there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity/utility. For example, the reference of Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York) teaches "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). The teachings of Branden et al. are exemplified by the reference of Witkowski et al. (*Biochemistry* 38:11643-11650), which teaches that only a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see *e.g.*, Table 1, page 11647).

The amount of direction provided by the inventor and The existence of working examples: The specification discloses only a single working example of a Fbp1 or a βTrcp2 polypeptide, *i.e.*, Fbp1 of SEQ ID NO:2 and βTrcp2 as disclosed by Kipreos and Pagano (*supra*). The specification fails to disclose any specific guidance for altering the polypeptide of SEQ ID NO:2 or the βTrcp2 as disclosed by Kipreos and Pagano (*supra*) with an expectation that the resulting variants as encompassed by the claims will maintain the desired activity/utility. Moreover, it is noted that the use of the claimed invention is in identifying a compound that is a "useful for the treatment of proliferative and differentiative disorders" and the specification fails to provide guidance for using

those compounds that may modulate the activity of a *variant* of SEQ ID NO:2 and/or the βTrcp2 as disclosed by Kipreos and Pagano (*supra*), but fail to have a similar effect on SEQ ID NO:2 or βTrcp2 as disclosed by Kipreos and Pagano (*supra*).

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating or generating variants of a polypeptide were known in the art at the time of the invention, it was not routine in the art to screen – by a trial and error process – for all polypeptides having a substantial number of modifications as encompassed by the claims for those that maintain "the activity" of SEQ ID NO:2 and/or the βTrcp2 as disclosed by Kipreos and Pagano (*supra*).

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, undue experimentation is necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[15] Claim(s) 7, 13-14, 16, and 29-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Yaron et al. (*EMBO J* 16:6486-6494, 1997). Claims 7, 13, 29, 31, 33, and 35 are drawn to a screening assay comprising contacting a compound with a cell or extract thereof expressing Fbp1, βTrcp2, and IKBα and detecting a change in the activity of Fbp1 or *β*Trcp2, optionally wherein the detecting is by detecting a change in the levels of IKBα protein. Claims 14, 16, 30, 32, 34, and 36 are drawn to a screening method comprising: a) contacting a compound with a cell or extract thereof expressing Fbp1, IKBα, and a test compound, and detecting a change in the activity of Fbp1; b) contacting a compound with a cell or extract thereof expressing βTrcp2, IKBα, and a test compound, and detecting a change in the activity of *β*Trcp2; and c) contacting a compound with a cell or extract thereof expressing Fbp1, βTrcp2, IKBα, and the test compound or compounds identified as changing the activity of Fbp1 or *β*Trcp2, and detecting a change in the activity of Fbp1 or *β*Trcp2.

The reference of Yaron et al. teaches a method for assaying degradation of phosphorylated IKBα protein in a reticulocyte extract in the presence and absence of ATP and in the presence of ATP and various peptides by measuring levels of IKBα protein by Western blotting (paragraph bridging pp. 6488-6489 and p. 6489, Figure 4), thus anticipating claims 7, 13, 33, and 35. Under the disclosed assay conditions, the level of phosphorylated IKBα is decreased in the presence of ATP or ATP and peptides ppFos or p21 as compared to the level of phosphorylated IKBα in the absence of ATP (compare Lanes 1 and 2 of Figure 4), thus anticipating claim 31. Also, the level of phosphorylated IKBα is increased in the presence of peptides pp21 and pp19 as compared to the level of phosphorylated IKBα in the absence of peptides pp21 and pp19 (compare Lane 2 with Lanes 3 and 4 of Figure 4), thus anticipating claim 29. Yaron et al. further teaches assaying the level of ubiquitinated phosphorylated IKBα in the presence of peptide pp19 (p. 6488, top and p. 6489, Figure 3B, compare Lanes 1 and 6) and also assaying the level of ubiquitinated phosphorylated IKBα in the presence of peptide pp21 and reticulocyte lysate fraction II (p. 6490, Figure 5A, compare Lanes 1 and 4), which resulted in an increase in ubiquitinated phosphorylated IKBα as compared to no peptide, which, in combination with the above cited teachings, anticipates claims 14, 16, 30, 32, 34, and 36.

[16] As noted above, the instant application claims priority under 35 USC § 120 to non-provisional application 10/652,928 and claims priority under 35 USC § 119(e) to provisional applications 60/098,355, filed on 8/28/1998, 60/118,568, filed on 2/3/1999,

and 60/124,449, filed on 3/15/1999. The examiner has reviewed these provisional applications for determining the priority date of the claimed invention. The examiner can find no support in these provisional applications for the invention as claimed. The following rejections are based on a priority date of 8/28/2003 for the claimed invention.

Claim(s) 7, 13-14, 16, and 29-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Yaron et al. (*Nature* 396:590-594, 1998; hereafter "Yaron 1998" to avoid confusion with the earlier cited Yaron et al. reference). The claims are drawn to screening methods as described above.

The reference of Yaron 1998 teaches a method for assaying the level of ubiquitination of phosphorylated IKBα protein or the level of phosphorylated IKBα protein in the presence or absence of a pp10 peptide, where the presence of pp10 decreased the level of ubiquitinated phosphorylated IKBα protein as compared to no peptide (p. 591, Figure 1, compare Lanes 6 and 7; p. 591, Figure 2, compare Lanes 3 and 4; and p. 592, Figure 4b, compare Lanes 2 and 3), thus anticipating claims 7, 13, 14, 16, and 31-36. Yaron 1998 further teaches a method for assaying the level of ubiquitination of phosphorylated IKBα protein or the level of phosphorylated IKBα protein in the presence or absence of IKK, where the presence of IKK increased the level of phosphorylated IKBα protein as compared to no IKK treatment (p. 592, Figure 4a, compare, *e.g.,* Lanes 1 and 2; p. 592, Figure 4b, compare, *e.g.,* Lanes 1 and 2; and p. 592, Figure 4c, compare, *e.g.,* Lanes 1 and 2), thus anticipating claims 7, 13, 14, 16, 29-30, and 33-36.

Conclusion

[17] Status of the claims:

- Claims 1-7, 11, 13-14, and 16-36 are pending.
- Claims 1-6, 11, and 17-28 are withdrawn from consideration.
- Claims 7, 13-14, 16, and 29-36 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656